

TOXICOLOGICAL PROFILE FOR BENZENE

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Agency for Toxic Substances and Disease Registry**

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DISCLAIMER

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UPDATE STATEMENT

A Toxicological Profile for benzene was released in April 1993. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

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FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.


The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;
- (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and
- (C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



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***Legislative Background**

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the *Federal Register* on April 29, 1996 (61 FR 18744). For prior versions of the list of substances, see *Federal Register* notices dated April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17, 1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); and February 28, 1994 (59 FR 9486). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

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THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. **Green Border Review.** Green Border review assures consistency with ATSDR policy.
2. **Health Effects Review.** The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.
3. **Minimal Risk Level Review.** The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.

PEER REVIEW

A peer review panel was assembled for benzene. The panel consisted of the following members:

1. Dr. Rogene Henderson, Biochemist, Lovelace Inhalation Toxicology Research Institute, Kirtland AFB, Albuquerque, New Mexico;
2. Dr. Carroll Snyder, Director, Laboratory of Inhalation Carcinogenesis and Toxicity, A.J. Lanza Laboratories, New York University, Tuxedo, New York; and
3. Dr. Gisela Witz, Professor, University of Medicine & Dentistry New Jersey (UMDNJ), Robert Wood Johnson Medical School, Department of Environmental and Community Medicine, Piscataway, New Jersey.

These experts collectively have knowledge of benzene's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

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1. PUBLIC HEALTH STATEMENT

This public health statement tells you about benzene and the effects of exposure.

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup. Benzene has been found in at least 816 of the 1,428 current or former NPL sites. However, it's unknown how many NPL sites have been evaluated for this substance. As more sites are evaluated, the sites with benzene may increase. This information is important because exposure to this substance may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact.

If you are exposed to benzene, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS BENZENE?

Benzene, also known as benzol, is a colorless liquid with a sweet odor. Benzene evaporates into air very quickly and dissolves slightly in water. Benzene is highly flammable. Most people can begin to smell benzene in air at 1.5–4.7 parts of benzene per million parts of air (ppm) and smell benzene in water at 2 ppm. Most people can begin to taste benzene in water at 0.5–4.5 ppm. Benzene is found in air, water, and soil.

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Benzene found in the environment is from both human activities and natural processes. Benzene was first discovered and isolated from coal tar in the 1800s. Today, benzene is made mostly from petroleum sources. Because of its wide use, benzene ranks in the top 20 in production volume for chemicals produced in the United States. Various industries use benzene to make other chemicals, such as styrene (for Styrofoam® and other plastics), cumene (for various resins), and cyclohexane (for nylon and synthetic fibers). Benzene is also used for the manufacturing of some types of rubbers, lubricants, dyes, detergents, drugs, and pesticides. Natural sources of benzene, which include volcanoes and forest fires, also contribute to the presence of benzene in the environment. Benzene is also a part of crude oil and gasoline and cigarette smoke. For more information on the nature and uses of benzene, see Chapters 3 and 4.

1.2 WHAT HAPPENS TO BENZENE WHEN IT ENTERS THE ENVIRONMENT?

Benzene is commonly found in the environment. Industrial processes are the main sources of benzene in the environment. Benzene levels in the air can increase from emissions from burning coal and oil, benzene waste and storage operations, motor vehicle exhaust, and evaporation from gasoline service stations. Since tobacco smoke contains high levels of benzene, tobacco smoke is another source of benzene in air. Industrial discharge, disposal of products containing benzene, and gasoline leaks from underground storage tanks can release benzene into water and soil.

Benzene can pass into air from water and soil surfaces. Once in the air, benzene reacts with other chemicals and breaks down within a few days. Benzene in the air can attach to rain or snow and be carried back down to the ground.

Benzene in water and soil breaks down more slowly. Benzene is slightly soluble in water and can pass through the soil into underground water. Benzene in the environment does not build up in plants or animals. For more information on what happens to benzene after it gets into the environment, see Chapters 4 and 5.

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1.3 HOW MIGHT I BE EXPOSED TO BENZENE?

Most people are exposed to a small amount of benzene on a daily basis. You can be exposed to benzene in the outdoor environment, in the workplace, and in the home. Exposure of the general population to benzene is mainly through breathing air that contains benzene. The major sources of benzene exposure are tobacco smoke, automobile service stations, exhaust from motor vehicles, and industrial emissions. Vapors (or gases) from products that contain benzene, such as glues, paints, furniture wax, and detergents can also be a source of exposure. Auto exhaust and industrial emissions account for about 20% of the total nationwide exposure to benzene. About 50% of the entire nationwide exposure to benzene results from smoking tobacco or from exposure to tobacco smoke. The average smoker (32 cigarettes per day) takes in about 1.8 milligrams (mg) of benzene per day. This is about 10 times the average daily intake of nonsmokers.

Background levels of benzene in air range from 2.8 to 20 parts of benzene per billion parts of air (ppb) (1 ppb is 1,000 times less than 1 ppm and equals about 3 micrograms of benzene in a cubic meter of air [$\mu\text{g}/\text{m}^3$]). People living in cities or industrial areas are generally exposed to higher levels of benzene in air than those living in rural areas. Benzene levels in the home are usually higher than outdoor levels. People living around hazardous waste sites, petroleum refining operations, petrochemical manufacturing sites, or gas stations may be exposed to higher levels of benzene in air.

For most people, the level of exposure to benzene through food, beverages, or drinking water is not as high as through air. Typical drinking water contains less than 0.1 ppb benzene. Benzene has been detected in some bottled water, liquor, and food. Leakage from underground gasoline storage tanks or from landfills and hazardous waste sites containing benzene can result in benzene contamination of well water. People with benzene-contaminated tap water can be exposed from drinking the water or eating foods prepared with the water. In addition, exposure can result from breathing in benzene while showering, bathing, or cooking with contaminated water.

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Individuals employed in industries that make or use benzene may be exposed to the highest levels of benzene. As many as 238,000 people may be occupationally exposed to benzene in the United States. These industries include benzene production (petrochemicals, petroleum refining, and coke and coal chemical manufacturing), rubber tire manufacturing, and storage or transport of benzene and petroleum products containing benzene. Other workers who may be exposed to benzene because of their occupations include steel workers, printers, rubber workers, shoe makers, laboratory technicians, firefighters, and gas station employees. For more information on how you might be exposed to benzene, see Chapter 5.

1.4 HOW CAN BENZENE ENTER AND LEAVE MY BODY?

Benzene can enter your body through your lungs when you breathe contaminated air. It can also enter through your stomach and intestines when you eat food or drink water that contains benzene. Benzene can enter your body through skin contact with benzene-containing products such as gasoline.

When you are exposed to high levels of benzene in air, about half of the benzene you breathe in leaves your body when you breathe out. The other half passes through the lining of your lungs and enters your bloodstream. Animal studies show that benzene taken in by eating or drinking contaminated foods behaves similarly in the body to benzene that enters through the lungs. A small amount will enter your body by passing through your skin and into your bloodstream during skin contact with benzene or benzene-containing products. Once in the bloodstream, benzene travels throughout your body and can be temporarily stored in the bone marrow and fat. Benzene is converted to products, called metabolites, in the liver and bone marrow. Some of the harmful effects of benzene exposure are believed to be caused by these metabolites. Most of the metabolites of benzene leave the body in the urine within 48 hours after exposure. For more information on how benzene can enter and leave your body, see Chapter 2.

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1.5 HOW CAN BENZENE AFFECT MY HEALTH?

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests.

One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

After exposure to benzene, several factors determine whether harmful health effects will occur and if they do, what the type and severity of these health effects might be. These factors include the amount of benzene to which you are exposed and the length of time of the exposure. Most data involving effects of long-term exposure to benzene are from studies of workers employed in industries that make or use benzene. These workers were exposed to levels of benzene in air far greater than the levels normally encountered by the general population. Current levels of benzene in workplace air are much lower than in the past. Because of this reduction, and the availability of protective equipment such as respirators, fewer workers have symptoms of benzene poisoning.

Brief exposure (5–10 minutes) to very high levels of benzene in air (10,000–20,000 ppm) can result in death. Lower levels (700–3,000 ppm) can cause drowsiness, dizziness, rapid heart rate, headaches, tremors, confusion, and unconsciousness. In most cases, people will stop feeling these effects when they stop being exposed and begin to breathe fresh air.

Eating foods or drinking liquids containing high levels of benzene can cause vomiting, irritation of the stomach, dizziness, sleepiness, convulsions, rapid heart rate, coma, and death. The health effects that may result from eating foods or drinking liquids containing lower

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levels of benzene are not known. If you spill benzene on your skin, it may cause redness and sores. Benzene in your eyes may cause general irritation and damage to your cornea.

Benzene causes problems in the blood. People who breathe benzene for long periods may experience harmful effects in the tissues that form blood cells, especially the bone marrow. These effects can disrupt normal blood production and cause a decrease in important blood components. A decrease in red blood cells can lead to anemia. Reduction in other components in the blood can cause excessive bleeding. Blood production may return to normal after exposure to benzene stops. Excessive exposure to benzene can be harmful to the immune system, increasing the chance for infection and perhaps lowering the body's defense against cancer.

Benzene can cause cancer of the blood-forming organs. The Department of Health and Human Services (DHHS) has determined that benzene is a known carcinogen. The International Agency for Cancer Research (IARC) has determined that benzene is carcinogenic to humans, and the EPA has determined that benzene is a human carcinogen. Long-term exposure to relatively high levels of benzene in the air can cause cancer of the blood-forming organs. This condition is called leukemia. Exposure to benzene has been associated with development of a particular type of leukemia called acute myeloid leukemia (AML).

Exposure to benzene may be harmful to the reproductive organs. Some women workers who breathed high levels of benzene for many months had irregular menstrual periods. When examined, these women showed a decrease in the size of their ovaries. However, exact exposure levels were unknown, and the studies of these women did not prove that benzene caused these effects. It is not known what effects exposure to benzene might have on the developing fetus in pregnant women or on fertility in men. Studies with pregnant animals show that breathing benzene has harmful effects on the developing fetus. These effects include low birth weight, delayed bone formation, and bone marrow damage.

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The health effects that might occur in humans following long-term exposure to food and water contaminated with benzene are not known. In animals, exposure to food or water contaminated with benzene can damage the blood and the immune system and can even cause cancer. See Chapter 2 for more information on the health effects resulting from benzene exposure.

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO BENZENE?

Several tests can show if you have been exposed to benzene. Some of these tests may be available at your doctor's office. All of these tests are limited in what they can tell you. The test for measuring benzene in your breath must be done shortly after exposure. This test is not very helpful for detecting very low levels of benzene in your body. Benzene can be measured in your blood. However, since benzene disappears rapidly from the blood, measurements may be accurate only for recent exposures. In the body, benzene is converted to products called metabolites. Certain metabolites of benzene, such as phenol, muconic acid, and S-phenyl-N-acetyl cysteine (PhAC) can be measured in the urine. The amount of phenol in urine has been used to check for benzene exposure in workers. The test is useful only when you are exposed to benzene in air at levels of 10 ppm or greater. However, this test must also be done shortly after exposure, and it is not a reliable indicator of how much benzene you have been exposed to, since phenol is present in the urine from other sources (diet, environment). Measurement of muconic acid or PhAC in the urine is a more sensitive and reliable indicator of benzene exposure. The measurement of benzene in blood or of metabolites in urine cannot be used for making predictions about whether you will experience any harmful health effects. Measurement of all parts of the blood and measurement of bone marrow are used to find benzene exposure and its health effects.

For people exposed to relatively high levels of benzene, complete blood analyses can be used to monitor possible changes related to exposure. However, blood analyses are not useful when exposure levels are low. For more information on tests for benzene exposure, see Chapters 2 and 6.

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1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed in not-to-exceed levels in air, water, soil, or food that are usually based on levels that affect animals, then they are adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors.

Recommendations and regulations are also periodically updated as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for benzene include the following:

EPA has set the maximum permissible level of benzene in drinking water at 5 parts per billion (ppb). Because benzene can cause leukemia, EPA has set a goal of 0 ppb for benzene in drinking water and in water such as rivers and lakes. EPA estimates that 10 ppb benzene in drinking water that is consumed regularly or exposure to 0.4 ppb benzene in air over a lifetime could cause a risk of one additional cancer case for every 100,000 exposed persons. EPA recommends a maximum permissible level of benzene in water of 200 ppb for short-term exposures (10 days) for children.

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EPA requires that the National Response Center be notified following a discharge or spill into the environment of 10 pounds or more of benzene.

The Occupational Safety and Health Administration (OSHA) regulates levels of benzene in the workplace. The maximum allowable amount of benzene in workroom air during an 8-hour workday, 40-hour workweek is 1 part per million (ppm). Since benzene can cause cancer, the National Institute for Occupational Safety and Health (NIOSH) recommends that all workers likely to be exposed to benzene wear special breathing equipment (NIOSH 1974). For more information on federal regulations, see Chapter 7.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333

* Information line and technical assistance

Phone: (404) 639-6000
Fax: (404) 639-6315 or 6324

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses resulting from exposure to hazardous substances.

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* To order toxicological profiles, contact:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Phone: (800) 553-6847 or (703) 487-4650